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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/388,221	09/01/1999	JOHN REED C	P-LJ-3650	3565

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EXAMINER
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ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/05/2002 27

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/388,221	Reed
Examiner	**Art Unit**
Anne Marie Wehbé	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 22, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 4-9, 11, 18, 27, 38, and 66-88* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 4-9, 11, 18, 27, 38, and 66-88* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continued Prosecution Application

The request filed on 7/22/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/388,221 is acceptable and a CPA has been established. As requested, applicant's amendment received on 3/28/02 has been entered. Claims 10, 12-17, 19-26, 28, 30-37, and 39-65 have been canceled. New claims 87-88 have been entered. Claims 1, 4-9, 11, 18, 27, 38, and 66-88 are pending and active in the instant application. An action on the CPA follows.

Those sections of Title 35, US code, not included in this action, can be found in the previous office action.

Claim Rejections - 35 USC § 112

The rejection of original, amended, or new claims 1, 5-9, 11, 18, 27, 38, 66-69, 71-74, and 77-88 under 35 U.S.C. 112, first paragraph, for lack of written description is maintained in part over claims 1, 5-7, 18, 38, 66-69, 71-74, and 83-86 and withdrawn over claims 8-9, 11, 27, 77-82, and 87-88. Applicant's arguments as they pertain to the remaining grounds of rejection have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below. As in the previous office action,

the applicant is again reminded that this rejection is a written description rejection which is separable from enablement. Applicant's arguments regarding the use of the disclosed nucleic acids for modulating apoptosis are not relevant to the rejection of the claims for written description and have been addressed in the response to applicant's argument regarding the lack of enablement of the claims, see below. The instant rejection concerns whether the specification provides a sufficient description of the nucleic acids and proteins claimed such that it would be clear that applicant was in possession of the invention at the time of filing.

The applicant argues that based on the claim amendments, the claimed nucleic acids must encode a polypeptide which forms a CARD domain fold. As such, the applicant argues that the CARD domain fold was known in the art, citing Qin et al. (Exhibit B), and that the skilled artisan would have known which residues could be varied, and how they could be varied, while retaining the CARD domain fold. The applicant also reiterates the argument set forth in previous responses that the specification teaches that the biologically relevant portions of a NAC protein are encoded by their NAC CARD and NAC NB-ARC domains and thus the skilled artisan would expect that extensive variation outside these domains would not affect NAC CARD and NAC NB-ARC activity. In response, it is noted that although the claims have been amended to recite that the nucleic acid forms a CARD domain fold, the claims do not recite that the nucleic acid forms an NB-ARC domain. In order for the nucleic acid to meet the claim limitations of encoding an NAC protein, both a functional NB-ARC and a functional CARD domain must be present. While applicant's argument regarding the "biological" activity of the CARD domain for binding other

CARD domain containing proteins is acknowledged, the claim still requires a NAC protein, and not simply a protein comprising a CARD domain fold. The specification does not provide a description of any functional biological activity of the disclosed NAC proteins which can serve to identify other proteins encoded by nucleic acid sequences other than SEQ ID NOS 1, 3, and 5 which are in fact NAC proteins and not simply a protein capable of binding to a CARD domain. The claims as written recite sequences with 80% sequence identity to specific SEQ ID NOS. It is unclear which of the numerous sequences which are encompassed by these claims would in fact encode a protein with both NB-ARC and CARD domain activity. Without a clear description of the particular biological activity of a NAC protein according to the instant invention and the particular sequence or structural characteristics associated with those biological activities, the specification fails to provide adequate written description for the scope of the claims as written.

As discussed in the previous office action, the specification fails to provide sufficient description as to any actual biological activity of the disclosed nucleic acid or amino acid sequence other than binding to apaf-1. The demonstration of binding to an NB-ARC or CARD domain in vitro does not demonstrate that the disclosed proteins naturally bind proteins containing these domains in vivo or that the binding results in any particular biological activity in any type of cell in a mammal. In regards to the post-filing article by Chu et al., previously submitted by applicant's as exhibit A, it is noted that the applicant has not identified whether the "NAC" disclosed by Chu et al. is identical to or encodes any of SEQ ID Nos: 1-6 or is at least 80% identical to SEQ ID Nos: 2, 4, of 6. While the specification describes nucleic acids consisting of

SEQ ID Nos: 1, 3, and 5 and nucleic acids encoding the predicted encoded amino acids consisting of SEQ ID Nos: 2, 4, and 6, the specification fails to identify the actual physical, chemical, and biological characteristics of these proteins such that it would be clear which nucleic acid or amino acid sequences that vary from the disclosed sequences would meet the claimed limitations of "NAC" activity. Further, it is well known in the art that even under high stringency conditions, numerous nucleic acid sequences will be capable of binding which are not 100% identical to the wild type sequence. The specification fails to describe the effects of any nucleic acid or amino acid changes on any biological activity of the proteins encoded by SEQ ID Nos: 1, 3, or 5, (SEQ ID Nos: 2, 4, or 6). Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). In the absence of any description of the biological activity of the encoded "NAC" proteins, SEQ ID Nos: 2, 4, and 6 (encoded by the nucleic acids SEQ ID Nos: 1, 3, and 5 respectively), the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides which may share those characteristics, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1602 at 1606 (CAFC 1993) and *Amgen*

Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. Therefore, in view of the lack of description of isolated nucleic acids encoding a biologically active NAC as detailed above, the specification does not meet the written description provision of 35 U.S.C. 112, first paragraph.

The rejection of original, amended, or new claims 1, 5-9, 11, 18, 27, 38, 66-69, 71-74, and 77-88 under 35 U.S.C. 112, first paragraph, for scope of enablement is maintained over claims 1, 5-7, 18, 38, 66-69, 71-74, and 83-86 and withdrawn over claims 8-9, 11, 27, 77-82, and 87-88. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons or record as discussed in detail below.

The previous office action stated that the specification, while being enabling for an isolated nucleic acid encoding an NB-ARC and CARD containing protein (NAC) selected from DNA consisting of SEQ ID Nos: 1, 3, or 5, or DNA encoding the amino acid sequences set forth in SEQ ID Nos: 2, 4, or 6, does not reasonably provide enablement for functional fragments of the above, DNA encoding a biologically active NAC which hybridizes to the DNA molecules identified above with high stringency, or which is degenerate to those nucleic acids, or for methods of modulating the level of apoptosis in a cell by introducing the above identified sequences into the cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The applicant reiterates the argument previously made that the specification and the prior art provide sufficient guidance concerning the NB-ARC and CARD protein domains that the skilled artisan would be able to predict without undue experimentation which amino acid and/or nucleic acid changes in any of SEQ ID Nos: 1-6 would result in a nucleic acid sequence encoding a protein with "NAC" activity. The specification teaches three novel mRNA splice variants whose protein coding region has regions homologous to an NB-ARC domain and a CARD domain. The specification also teaches that these domains are capable of homodimerization and are further capable of interacting in vitro with the NB-ARC or CARD domains respectively of other "NAC" proteins such as CED-4. The demonstration of binding to an NB-ARC or CARD domain *in vitro*, however, does not demonstrate that the disclosed proteins naturally bind proteins containing these domains in vivo or that the binding results in any particular biological activity in any type of cell in a mammal. According to the specification's definition of a "NAC" protein as a protein which comprises an NB-ARC domain and a CARD domain, many NAC proteins were reported in the art at the time of filing. These proteins differ in their biological properties and functional activity. Some inhibit apoptosis, some induce apoptosis, and some have **no** effect on apoptosis but rather affect cytokine expression and inflammatory reactions. Aside from demonstrating in vitro protein:protein interactions between the novel NB-ARC and CARD domains of the instant invention and several taught by the art, the specification does not provide any guidance as to any specific biological activity of the novel "NAC" proteins encoded by the disclosed cDNA or demonstrate that any of the disclosed proteins or protein domains or fragments have any

apoptosis modulating activity either in vitro or in vivo. Several publications document the unpredictability of attributing function based on sequence similarity. See in particular Gerhold et al. (1996) BioEssays, Vol. 18, No. 12, 973-981, Wells et al. (1997) J. Leuk. Biol., Vol. 61 (5), 545-550, and Russell et al. (1994) J. Mol. Biol., Vol. 244, 322-350. Thus, the sequence similarity between the disclosed "NAC" sequences and proteins with known biological activities such as CED-4 does not overcome the unpredictability of determining the biological activity of a particular protein sequence in the absence of factual evidence.

Furthermore, it was well known at the time of filing that for nucleic acids as well as for proteins even a single nucleotide or amino acid change or mutation can destroy or substantially change the function of the biomolecule. The effects of these changes are largely unpredictable as to which ones will have a significant effect on structure, folding, activity etc. For example, Ding et al. teaches that a single conservative amino acid substitution of alanine with isoleucine in IL-10 converts the protein to an immunostimulatory rather than an immunoinhibitory molecule and that "this single conservative residue alteration significantly affects ligand affinity for receptor". Thus, it is clear that the skilled artisan at the time of filing would not have considered it predictable whether even a single amino acid change would result in a protein with identical function to the original protein. In the absence of any teachings as to the specific biological activities of the proteins encoded by SEQ ID Nos: 1, 3, or 5, it would have required undue experimentation to determine which of the numerous possible sequences which have between 80-95% sequence homology to SEQ ID Nos: 2, 4, or 6 would have the same biological activity as the wild type

sequences. Thus, in the absence of any specific teachings in the specification concerning the actual biological properties of the predicted polypeptides encoded by SEQ ID Nos. 1, 3, or 5, or set forth in SEQ ID NOS: 2, 4, or 6, the art recognized unpredictability of attributing particular function properties to a polypeptide based on sequence similarity, the art recognized differences in function between proteins containing NB-ARC and CARD domains, and the breadth of the claims, it would have required undue experimentation to practice the scope of the invention as claimed.

In regards to methods of modulating apoptosis in cell in vivo or in vitro by transfecting said cells with a nucleic acid encoding a NAC or functional fragment thereof, the applicant again argues that post-filing evidence previously provided as a publication by Chu et al. (2001), exhibit A, demonstrates that both full length NAC and a fragment of NAC encoding the NAC CARD domain can modulate apoptosis in cell in tissue culture. It is again noted that the applicant has not identified whether the "NAC" disclosed by Chu et al. is identical to or encodes any of SEQ ID Nos: 1-6 or is at least 80% identical to SEQ ID Nos: 2, 4, of 6. Regardless, Chu et al. teaches that overexpression of a full length NAC is associated with Apaf-1 mediated apoptosis only in the presence of overexpressed Apaf-1 AND pro-Casp9 or overexpressed Apaf-1 and an Apaf-1 apoptosis inducer. Likewise, Chu et al. teaches that the NAC CARD domain inhibits Apaf-1 apoptosis only in the presence of overexpressed Apaf-1 AND pro-Casp9 or overexpressed Apaf-1 and an Apaf-1 apoptosis inducer. The overexpression of the full length NAC or the NAC CARD domain alone did NOT modulate apoptosis. The instant specification neither discloses nor claims

the modulation of apoptosis by the expression of NAC or NAC CARD AND Apaf-1 AND pro-Casp9 or an Apaf-1 apoptosis inducer. Thus, a nexus cannot be drawn between the teachings of Chu et al. and the instant invention as claimed. Please note as well, that the claims as written are broad and recite the modulation of apoptosis in any type of cell. While the applicant states that the skilled artisan would choose to use cells which overexpress apoptosis modulators such as Apaf-1 and caspace-9, these limitations are not present in the claims, and since, in patentability context, claims are to be given their broadest reasonable interpretations, limitations are not to be read into claims from the specification. *In re Van Guens*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Please note as well that a feature which is taught as critical to the invention and is not recited in the claims should result in a rejection of such claim under the enablement provision section of 35 U.S.C. 112. See *In re Mayhew* , 527 F.2d 1229,1233, 188 USPQ 356, 358 (CCPA 1976).

In regards to the predictability of using any and all vectors to express therapeutic levels of gene expression in vivo, the applicant reiterates the argument that the post-filing reference provided with the previous response, Roth et al. (1999), supports predictability of gene therapy using vector mediated gene delivery before the filing of the instant invention. As noted in the previous office action, the Roth et al. publication, exhibit B, simply teaches that adenovirus mediated p53 delivery to tumors in vivo in combination with chemotherapy or radiation therapy shows promising results in early clinical trials. The teachings of Roth et al. are limited to the treatment of cancer using p53. A nexus between adenoviral p53 treatment of cancer and the

applicant's methods cannot be drawn as p53 and "NAC" do not share any known biological functions. The applicant now argues that NAC and p53 share the biological activity of "modulating" apoptosis. Neither Roth et al. nor the art at the time of filing teaches or demonstrates that p53 contains NB-ARC and CARD domains, or is capable of binding to apaf-1. p53 is a tumor suppressor gene with very particular and well defined biological activities. The specification does not teach or provide any concrete support that the disclosed NAC proteins share any of the p53 protein's known biological activities. Further, as noted above, neither the specification nor the post-filing evidence provided actually demonstrates that a NAC protein according to the instant invention either induces or inhibits apoptosis in any particular type of cell.

Further, the claims are not limited to cancer therapy or the administration of any particular vector. Roth et al. makes no statements as to the general predictability of gene therapy. In fact, Roth et al. clearly states in regards to gene therapy as a strategy of disease treatment that, " while conceptually simple, this strategy of gene replacement therapy is proving to have practical complexities that make its clinical implementation more difficult than had been anticipated. Currently available vectors have been unable to sustain high enough levels of gene expression over long enough of time" (Roth, page 148, column 1). Thus, it is clear that as of 1999, gene therapy of disease was not considered predictable by the skilled artisan, and that Roth et al. supports the conclusions of the previously cited prior art references Orkin et al., Verma et al., and Marshall et al.

Claims 8-9, 11, 27, 77-81, and 87-88 are **newly** rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly FP. The applicant has amended claims 8-9 and 77-81 to recite an oligonucleotide "consisting of" at least 20 or 30 contiguous nucleotides as set forth in various SEQ ID NOS or fragments of SEQ ID NOS, "said oligonucleotide optionally having additional nucleotides at the 5' or 3' end that differ from the nucleotide sequence" previously recited. The language "consisting of" is considered "closed" claim language. However, the amendments to the claims to recite wherein the oligo may "optionally" have additional nucleotides renders the claim more open and thus indefinite since it is now unclear what the metes and bounds of the claim are despite the use of the words "consisting of". It is unclear how many "additional nucleotides" at the 5' or 3' end may be added to the specifically claimed sequences and still meet the claim limitations. Further, the presence of an additional unknown number of nucleotides is inconsistent with the use of the term "consisting of". As such the claims as a whole, and those claims which depend on the amended claims, are indefinite.

Claim Objections

The objections to claims 9 and 27 under 37 CFR 1.75(c) as being in improper form are withdrawn in view of applicant's amendments to the claims.

Claim Rejections - 35 USC § 102

The rejection of amended or new claims 8 and 77-82 under 35 U.S.C. 102(a) over Nagase et al. is withdrawn in view of applicant's amendments to the claims. However, please note that applicant's amendment to claim 8 has resulted in new grounds of rejection under 35 U.S.C. 102 and 103, see below.

Claim 8 is **newly** rejected under 35 U.S.C. 102(b) as being anticipated by GSS sequence submission B33808 to the gp_gss sequence database, 10/17/97, defined as HS-1023-A2-D09-MF.abi CIT Human Genomic Sperm Library genomic clone. The applicant claims an oligonucleotide consisting of at least 30 -1035 contiguous nucleotides of SEQ ID NO:1, and optionally additional nucleotides that differ from SEQ ID NO:1.

The genomic sequence submission B33808 consists of 479 nucleotides. 420 contiguous nucleotides of this sequence shares 100% sequence identity with SEQ ID NO:1 from nucleotides 1882-2301. The B33808 sequence has 59 additional nucleotides which do not match SEQ ID NO:1. Thus, by meeting all the limitations of the claim as written, GSS sequence submission B33808 anticipates the instant claim.

Claim 82 is **newly** rejected under 35 U.S.C. 102(b) as being anticipated by EST sequence submission H51863 to the gp_est2 sequence database, 9/18/95, defined as yp83f08.r1 Soares fetal

liver spleen 1NFLS Homo Sapiens. The applicant claims an oligonucleotide comprising at least 20 contiguous nucleotides of the nucleotide sequence set forth as nucleotides 3784-3915 of SEQ ID NO:1.

The H51863 sequence is 477 nucleotides, of which 74 contiguous nucleotide share 100% sequence identity with nucleotides 3784-3860 of SEQ ID NO:1. Since applicant's claim use the broad language "comprising", the claimed oligonucleotide encompasses any oligonucleotide which has at least 20 contiguous nucleotides in common with nucleotides 3784-3860 of SEQ ID NO:1. The H51863 nucleotide sequence has the recited limitations and thus anticipates the instant claim.

Claim Rejections - 35 USC § 103

The rejection of amended claims 9, 11, and 27 under 35 U.S.C. 103(a) over Nagase et al. (1999) DNA Res. Vol. 6, 63-70 in view of Nagase et al. (1998) DNA Res. Vol. 5, 277-286. is withdrawn over claims 9, 11, and 27, and **newly applied** to claim 8. Applicant's arguments, as directed to the rejection of claims 9, 11, and 27, do not apply to the new grounds of rejection of claim 8.

The applicant's claim as amended recites an oligonucleotide consisting of at least 30 -1035 nucleotides of SEQ ID Nos: 1, 3, and 5. Nagase et al. teaches novel cDNA clones from human brain cDNA libraries which have large regions (>2800 bp) of 100% sequence identity to SEQ ID

Nos: 1, 3, and 5 (see page 66, Table 2) and which are part of the HUGE human sequence database. Nagase et al. further teaches the use of RT-PCR ELISA for identifying the expression pattern of the novel cDNAs in various cell types. While Nagase et al. does not disclose in this publication the characteristics of the oligos used in the RT-PCR ELISA assay, Nagase et al. teaches that the details of the methodology used can be found in a previous publication by the authors, Nagase et al. (1998) DNA Res. Vol. 5, 277-286. This referenced publication teaches that the oligonucleotides are labeled with digoxigenin (DIG)-11-dUTP and that the exact sequences of the primers used can be obtained from the authors. In fact, the sequences of all the primers used by the authors in generating the HUGE database are available on the internet at www.kazusa.or.jp. The disclosed oligomers are 21mers.

While Nagase et al. does not specifically teach oligomers which are 30mers or greater, Nagase et al. clearly teaches the use of labeled oligonucleotides derived from the fully disclosed sequence taught in the Nagase (1999) publication. The exact sequences of the oligos used by Nagase et al. are available in the HUGE database or from the authors directly at the time of filing. However, the exact sequence of the oligos is not required to render the instant invention obvious as the entire sequence of the novel cDNA identified by Nagase et al. was clearly disclosed in the 1999 publication. Based on the high degree of skill in the art of making oligonucleotides of variable length, including oligos greater than 30 nucleotides, suitable for RT-PCR at the time of filing, and the teachings of Nagase et al. that labeled oligos were successful in RT-PCR detection of the full length cDNA, it would have been *prima facie* obvious to the skilled artisan at the time

of filing to use oligonucleotide sequences greater than 30 nucleotides derived from the full length cDNA disclosed by Nagase et al. to detect the full length cDNA. Absent specifically identified secondary considerations, the skilled artisan would have considered probe lengths of 21 versus 30 oligonucleotides to be equivalent in terms of efficacy in detecting the larger sequence as disclosed by Nagase et al. Thus, absent evidence to the contrary, the skilled artisan would have had a reasonable expectation of success in detecting the full length cDNA disclosed by Nagase et al. with a labeled 30mer portion of the disclosed cDNA.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Thurs and every other Friday from 9:30-7:00. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER